

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A23K 1/14, 1/16	A1	(11) International Publication Number: WO 97/10723 (43) International Publication Date: 27 March 1997 (27.03.97)
(21) International Application Number: PCT/HU96/00048 (22) International Filing Date: 30 August 1996 (30.08.96) (30) Priority Data: P 95 02766 21 September 1995 (21.09.95) HU (71)(72) Applicants and Inventors: KÉKES-SZABÓ, András [HU/HU]; Petőfi u. 5, H-7171 Sióagárd (HU). FARKAS, Tibor [HU/HU]; Csaba u. 9/A, H-6723 Szeged (HU). DE ATZEL, Edward [HU/HU]; Petőfi u. 5, H-7171 Sióagárd (HU). TÖRÖK, Csaba [HU/HU]; Petőfi u. 5, H-7171 Sióagárd (HU). NAGYNE FARKAS, Rita [HU/HU]; Csaba u. 9/A, H-6723 Szeged (HU). KÉKES-SZABÓ, Ferenc [HU/HU]; Erdő 86, H-6080 Szabadszállás (HU). KULCSÁR, Erika [HU/HU]; Petőfi u. 5, H-7171 Sióagárd (HU). (74) Agent: INTERINNO PATENT OFFICE; Margit krt. 73., H-1024 Budapest (HU).		(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: FEED ADDITIVES HAVING PHYSIOLOGICALLY FAVOURABLE EFFECT		
(57) Abstract <p>The invention relates to a feed additive having physiologically favourable effect and a process for the preparation thereof. The said feed additive comprises grist of flaxseed or grist of soybean or grist of canolaseed or grist of perillaseed or flaxseed oil press cake or flaxseed oil applied to a carrier and further, optionally 0,001-1 % by weight of vitamin E, 0,001-1 % by weight of bile acid, and on the surface of the solid material 0,5-5 % by weight of paraffin or wax or palmitic acid or stearic acid or a mixture thereof, or natural or synthetic polymer and 0,1-5 % by weight of known auxiliary materials. The process for the preparation of the feed additive according to the invention comprises mixing grist of flaxseed or grist of soybean or grist of canolaseed or grist of perillaseed or granulated flaxseed oil press cake or flaxseed oil applied to a granulated carrier and, optionally 0,001-1 % by weight of vitamin E and 0,001-1 % by weight of bile acid and coating the mixture obtained with 0,5-10 % by weight of a mixture consisting of paraffin or wax or palmitic acid or a mixture thereof, or natural or synthetic polymer, 0,2-1 % by weight of surface-active material and optionally vitamin E, bile acid, solvent.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

FEED ADDITIVES HAVING PHYSIOLOGICALLY FAVOURABLE EFFECT

The invention relates to a feed additive having
5 physiologically favourable effect and to a process for
the preparation thereof.

Though cholesterol performs important biological tasks in
the body, it is the public enemy No. 1 in our age.

In case, it is present in excess in the human body, it
10 will deposit in the vessel walls, because of this the
vessel walls become rigid, the blood pressure increases,
or, if the deposited particles come off the vessel walls
for some reason, the vessel may get occluded, and if this
happens in the coronary artery or other vessels, it leads
15 to death.

In many countries, also in Hungary, the ratio of
myocardial infarction can amount up to 50% of causes of
death.

It has been observed that in countries where people
20 consume a lot of fish, the ratio of myocardial infarction
is rather low.

This is unambiguously attributed to the so-called omega-3
polyunsaturated fatty acids being present in the fish
lard in higher quantity.

25 In these fatty acids the first double bond is located at
the third carbon atom, counted from the methyl end of the
molecule, and the double bonds are in divinyl-methane

rithm. Western diet contains nil or very small quantity of omega-3 fatty acids. The most frequently consumed olive oil, sunflower oil or lard contains no omega-3 fatty acid, though for humans, 0,4-0,5% of the ingested 5 calories must be in such a form (Sardesi, V. M., J. Nutr. Biochem. 3, 155-166, 1992).

These omega-3 polyenoic acids decrease platelet aggregation, lower the cholesterol and triglyceride serum level, inhibit the deposition of cholesterol into the vessel 10 walls, and additionally, they are important components of the central nervous system, e.g. they are essential for the normal function of the brain. Purified fish oil is available in encapsulated form.

The world's fish oil production is about 1-2 million 15 metric ton per year, but most of it is used for other purposes, so according to estimations, the needs of only 80-100 millions of people can be filled, though a multiple number of humans are arteriosclerotic and exposed to the risk of infarction. Anyhow, it seems to 20 be justified to provide alternative omega-3 sources, taking into consideration the fact, that many people dislike fish oil preparations.

The most simple omega-3 polyunsaturated fatty acid is the linolenic acid (3,6,9-octadecatrienoic acid, 18:3 omega-3 25 or n-3), the animal body uses this acid for building up the long chain polyunsaturated omega-3 fatty acids.

A number of plants (perilla, flax, soybean, canola, nut)

have seeds rich in linolenic acid.

The beneficial biological effects of linolenic acid were shown also by Cunanan et al. (Brit. J. Nutr. 69, 443-453, 1993).

5 Thus, it seems to be obvious to feed the various domestic animals with these seeds or the oil obtained from them, provided in a suitable form, because in the animal body this fatty acid or its different derivatives accumulate, and the products obtained from the animals (meat, milk, 10 egg etc.) can be used for nutrition purposes. Certain preliminary data prove that a relatively low linolenic acid quantity brought into the human body, reduces the cholesterol level and also the risk of myocardial infarction (de Loregil, M. et al., The Lancet, 343, 15 1454-1459, 1994).

In this way, since a number of countries have no sea-fishery, the beneficial effects of the omega-3 fatty acids could be extended to great masses of the people. We had tried experiments, where animals were fed with 20 feed containing additive rich in linolenic acid. We have found that in the animal products, such as lard, meat, liver, milk, egg, the linolenic acid accumulated to a certain degree.

However, we could hardly detect this effect in case of 25 cows, because the linolenic acid was hydrogenated in the rumen and so it lost its advantageous effect. This biohydrogenation takes place in the body of other animals

too, though at a lower degree.

Experiments were carried out in order to supply feed, containing linolenic acid, with a proper cover preventing the autooxydation.

5 We have found that when the grounded flaxseed or other seeds or the flaxseed oil applied to a carrier which was then granulated, was covered with a material of high molecular weight, preferably with paraffin, wax, fatty acid of higher number of carbon atoms, a polymer, the
10 hydrogenating effect experienced in the animal body disappeared or significantly decreased.

The subject of the invention therefore a feed additive having physiologically favourable effect, which comprises grist of flaxseed or grist of soybean or grist
15 of canolaseed or grist of perillaseed or flaxseed oil press cake or flaxseed oil applied to a carrier, optionally 0,001-1% by weight of vitamin E, 0,001-1% by weight of bile acid and on the surface of the solid material 0,0-5% by weight paraffin or wax or palmitic
20 acid or a mixture thereof or natural or synthetic polymer and 0,1-5% by weight of known auxiliary materials.

The polymer is preferably cellulose acetate, gelatine, polyvinyl alcohol, polyvinyl alcohol acetate.

A further object of the invention is a process for the
25 preparation of said feed additive. The process according to the invention comprises mixing grist of flaxseed or grist of soybean or grist of canolaseed or grist of

perillaseed or granulated flaxseed oil press cake or
flaxseed oil applied to a granulated carrier, optionally
0,001-1% by weight of vitamin E and 0,001-1% by weight of
bile acid and coating the mixture with 0,5-10 % by weight
5 of a mixture consisting of paraffin or wax or palmitic
acid or a mixture thereof or natural or synthetic
polymers, 0,2-1% by weight of surface-active material and
optionally vitamin E, bile acid, solvent.

The additive according to the invention can be used as
10 feed additive for pig, cow, layer, fish and kinds of
fish.

The feed additive and the process for its preparation are
illustrated by the following examples.

15 Example 1

The flaxseed was grounded and the coat was applied within
48 hours.

After grinding the flaxseed had the following particle
size distribution:

20	2,0 mm	2,2 % by weight
	0,8 mm	62,0% by weight
	0,5 mm	20,7% by weight
	0,2 mm	9,1% gy weight
	under 0,2 mm	5,0 % by weight

25 The composition of the material used for coating the
flaxseed was the following:

98,2% by weight of paraffin of food industry grade (K 30/95 MOL Rt.) (softening point: 65°C)

1,5% by weight of HOCHST WACHS KP-301 (product of HOECHST)

5 0,3% by weight of TWEEN 80 emulgeator (product of ATLAS)

The quantity of the coating material applied was 6 parts by weight to 100 parts by weight of grist.

The coating process involved the following steps:

10 The grist of flaxseed was warmed to 75-95°C.

The homogenized coating mixture was warmed to 75°C and then added to the grist under continuous stirring. The stirring was continued until the coating material distributed homogenously on the surface of the flaxseed
15 grist. During this time the temperature of the mixture was maintained at 90°C.

After the mixture became completely homogenous the grist was cooled to room temperature.

The coating was carried out in a single-worm blending
20 equipment consisting of a heated section and a cooled one. For heating to the suitable temperature electric heating element and for cooling water counterflow was used.

25 Example 2

The process described in Example 1 was followed with the exception that for coating a mixture containing 0,1% by

weight of vitamin E and 0,2% by weight of bile acid was used.

Example 3

5 The process described in Example 1 was followed with the exception that instead of the grist of flaxseed starting material bran granules were used to which flaxseed oil was applied. The flaxseed oil content of the granules was 30% by weight and it also contained 0,001% by weight of
10 vitamin E and 0,1% by weight of bile acid.

Example 4

The process described in Example 1 was followed with the exception that grist of perillaseed was substituted for
15 the grist of flaxseed.

Example 5

A group of 50 pigs was fed for one month with a feed containing 20% of feed additive according to Example 1.
20 The control group consisting of 50 pigs was fed with the usual feed for one month.

The composition of fatty acids was determined in the lard, meat and liver of the animals.

The results are given in the following table.

	Fatty acid	Number of C =	Lard		Ham		Chop		Chuck		Liver	
			C		C	T	C	T	C	T	C	T
5	Myristic acid	14:0	1,9	1,6	1,8	1,4	1,3	1,4	1,9	1,4	-	-
	Palmitic acid	16:0	21,3	20,3	20,0	19,1	20,6	19,5	19,5	18,0	11,8	12,7
10	Palmitoleic acid	16:1 n-7	6,0	4,8	4,4	3,2	3,8	3,3	4,4	3,3	1,4	1,7
	Stearic acid	18:1	52,5	5,7	46,3	8,1	10,4	8,8	8,4	7,2	24,1	14,9
	Oleic acid	18:1 n-9	52,5	40,6	46,3	32,7	35,3	38,0	30,3	35,8	15,1	24,4
15	Linoleic acid	18:2 n-6	12,7	14,0	15,3	16,2	15,4	12,7	18,6	15,3	12,4	15,0
	Linolenic acid	18:3 n-3	1,0	10,7	1,5	9,4	0,7	8,3	1,7	10,2	1,1	11,4
20	Arachidonic acid	20:4 n-6	-	-	3,8	3,3	4,7	1,8	6,6	2,7	7,4	5,6
	Docosahexaenoic acid	20:5 n-3	-	-	-	0,7	-	0,5	-	0,6	2,3	7,7
25		n-6/n3	12,7	1,3	12,7	1,9	28,7	1,6	14,8	1,6	8,8	1,1
		n-3/n-6	0,08	0,76	0,07	0,51	0,03	0,51	0,06	0,60	0,11	0,92

C = Control

30 T = Treated

The results show that in the lard, meat and liver of animals fed with a feed containing the additive according to the invention, the quantity of linolenic acid increased compared to the control.

35 Example 6

A group of 100 layers was fed with conventional feed containing 25% by weight of feed additive according to Example 2.

The number of layers in the control group was also 100 and the animals were fed with conventional feed containing no additive.

The eggs layed by the animals involved in the experiment 5 were examined for the fatty acid composition. The results obtained are given in the following table.

Fatty acid composition of eggs
(% by weight)

	Control	Treated	
		15 days	21 days
Palmitic acid 16:0	26.4	21.6	23.3
Stearic acid 18:0	6.6	6.0	6.1
Oleic acid 18:1n-9	46.4	42.6	43.5
Linoleic acid 18:2n-6	10.0	8.5	8.7
Linolenic acid 18:3n-3	0.3	17.2	15.8
Arachidonic acid 20:4n-6	2.9	1.4	2.0
22:6n-3	0.8	2.2	2.6
Docosahexaenoic acid n-6/n-3	11.7	0.53	0.58
n-3/n-6	0.08	1.86	1.71

20 The results show that in the eggs layed by the animals of the test group the linolenic acid content significantly increased.

Example 7

25 An experimental group of 30 cows was fed for 60 days with a feed containing feed additive according to Example 1. The animals consumed from this feed twice a day such a

quantity which contained 2 x 500 g of additive according to Example 1. The fatty acid composition of the milk was examined. The results which are the means of 5 separate determinations are given in the following table.

5

Fatty acid composition of cow's milk

Fatty acid (number of C atoms: number of double bonds)	Control % by	Treated weight
Capric acid 10:0	2,8	4,2
Lauric acid 12:0	2,7	4,6
Myristic acid 14:0	10,5	13,5
Palmitic acid 16:0	31,2	23,8
Palmitoleic acid 16:1	2,6	2,1
Stearic acid 18:0	10,6	6,7
Oleic acid 18:1n-9	28,1	32,6
Linoleic acid 18:2n-6	2,9	6,4
Linoleic acid 18-3n-6	0,6	2,6
Eicosenoic acid 20:1n-9	0,5	2,2

10

It can be seen that the level of 18:0 acid decreased by 33% by weight, while that of 18:2 and 18:3 acids rose by 100% by weight and 400% by weight, respectively in the milks of experimental animals. Both, the reduction in 18:0 acid and the increase in 18:2 and 18:3 acids indicate a reduction of biohydrogenation processes taking place in the rumen.

15

What we claim is:

1. A feed additive having physiologically favourable effect which comprises grist of flaxseed or grist of soybean or grist of canolaseed or grist of perillaseed or 5 flaxseed oil press cake or flaxseed oil applied to a carrier and further, optionally 0,001-1% by weight of vitamin E, 0,001-1% by weight of bile acid, and on the surface of the solid material 0,5-5% by weight of paraffin or wax or palmitic acid or a mixture thereof, or 10 natural or synthetic polymer and 0,1-5% by weight of known auxiliary materials.

2. The feed additive according to Claim 1, wherein the polymer is cellulose acetate, polyvinyl alcohol, polyvinyl alcohol acetate.

15 3. Process for the preparation of feed additive, which comprises mixing grist of flaxseed or grist of soybean or grist of canolaseed or grist of perillaseed or granulated flaxseed oil press cake or flaxseed oil applied to a granulated carrier, and optionally 0,001-1% 20 by weight of vitamin E and 0,001-1% by weight of bile acid, and coating the mixture obtained with 0,5-10 % by weight of a mixture consisting of paraffin or wax or palmitic acid or a mixture thereof or natural or synthetic polymer, 0,2-1% by weight of surface-active 25 material, and optionally vitamin E, bile acid, solvent.

INTERNATIONAL SEARCH REPORT

International Application No
PC 1/HU 96/00048

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A23K1/14 A23K1/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A23K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 658 313 (DOX-AL ITALIA) 21 June 1995 see page 2, column 2, line 29 - page 3, column 4, line 7 see examples 1,2,4,5,10,14 see claims 1-6	1,3
Y	EP,A,0 363 733 (DOX-AL ITALIA) 18 April 1990 see page 2, line 42 - page 3, line 44 see examples 1,2 see claims 1,4-6,12-26 --- -/-	1-3

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

15 January 1997

Date of mailing of the international search report

29.01.97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

Dekeirel, M

INTERNATIONAL SEARCH REPORT

International Application No

PC1/HU 96/00048

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DE,A,43 01 736 (WOOBANG LAND CO. LTD.) 29 July 1993 see page 5, line 16 - line 24 see page 5, line 52 - line 60 see example 1 see claims 1-11 ---	1-3
A	EP,A,0 197 188 (DOX-AL ITALIA) 15 October 1986 see examples 1-4 see claims 1,3,15 ---	1,3
A	US,A,5 069 903 (PAUL A. STITT) 3 December 1991 see claim 1 ---	1,3
A	GB,A,2 137 881 (NOVOTRADE RT) 17 October 1984 see page 2, line 13 - line 26 ---	1,3
A	US,A,4 357 358 (RUDOLF SCHANZE) 2 November 1982 see examples 7-10 see claims 1,11 ---	1,3
A	AU,B,631 010 (AUSTRALIAN FEED CO. PTY. LIMITED) 12 November 1992 see claims 1-14 ---	1
A	DATABASE WPI Week 8312 Derwent Publications Ltd., London, GB; AN 83-28378K XP002022786 & JP,A,58 023 754 (NISSHIN FLOUR MILL KK) , 12 February 1983 see abstract -----	1

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PC1/HU 96/00048

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-658313	21-06-95	AU-A- 8161494 CA-A- 2138443	22-06-95 18-06-95
EP-A-363733	18-04-90	DE-D- 68911832 DE-T- 68911832 ES-T- 2048257	10-02-94 14-04-94 16-03-94
DE-A-4301736	29-07-93	CA-A- 2087792 JP-B- 2503352 JP-A- 6086641	24-07-93 05-06-96 29-03-94
EP-A-197188	15-10-86	AU-B- 586237 CA-A- 1281586 JP-C- 1700290 JP-B- 3051385 JP-A- 61242546	06-07-89 19-03-91 14-10-92 06-08-91 28-10-86
US-A-5069903	03-12-91	CA-A- 1336553 US-A- 5110592	08-08-95 05-05-92
GB-A-2137881	17-10-84	BE-A- 899369 DE-A- 3414330 FR-A- 2544199 JP-A- 60041447 NL-A- 8401217 SE-B- 459840 SE-A- 8402088 US-A- 4622341	09-10-84 29-11-84 19-10-84 05-03-85 01-11-84 14-08-89 15-10-84 11-11-86
US-A-4357358	02-11-82	DE-A- 2643093 DE-A- 2737295 AT-B- 354234 AU-B- 519721 AU-A- 2898577 BE-A- 859010 CA-A- 1107121 CH-A- 628214 FR-A- 2365299 GB-A- 1581281 NL-A- 7710095	30-03-78 01-03-79 27-12-79 17-12-81 29-03-79 16-01-78 18-08-81 26-02-82 21-04-78 10-12-80 29-03-78

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/HU 96/00048

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
---	---------------------	----------------------------	---------------------

US-A-4357358

SE-B- 433697

12-06-84

SE-A- 7710562

25-03-78

AU-B-631010

12-11-92

AU-A- 6264490

21-03-91